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PATENT

**IN THE UNITED STATES PATENT AND
TRADEMARK OFFICE**

Applicant(s): John F. Stone

Docket No.: 36435.0100

Serial No.: 09/498,135

Filed: February 4, 2000

Examiner: Enewold, T.

Title: CHROMOSOME-BASED METHOD FOR
FACILITATING DISEASE DIAGNOSIS

Group Art 1655
Unit:

RESPONSE AND AMENDMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

Dear Sir:

Applicant hereby responds to the Office Action dated May 31, 2000, for which the period to respond is extended by one month to September 30, 2000. Because September 30, 2000 fell on a Saturday, this Response and Amendment is timely filed on the following Monday, October 2, 2000. Please consider the following claim amendments.

In the Claims

Please amend claims 1, 11, and 16-17 as follows.

- BI
1. (Amended) A method suitable for facilitating disease diagnosis, ~~the method~~ comprising the steps of:
- exposing cells of a [suspected diseased] patient, suspected of having a disease for which chromosome damage is diagnostic, to a chromosome damaging agent selected to damage chromosomes within the nuclei of the cells to produce chromosome fragments;
 - marking at least some of the chromosome fragments; and
 - analyzing the marked chromosome fragments within cell nuclei to determine whether the cells were affected by the disease.

Sub
B2
A2

11. (Amended) A method for analyzing an effect of disease on cells, the method comprising the steps of:

- preparing cells suspected of being ~~[diseased]~~ affected by a disease for which chromosome damage is diagnostic by exposing the cells to a chromosome breakage agent to form chromosome pieces within nuclei of the cells;
- marking at least a portion of the chromosome pieces within the cells' nuclei;
- counting a number of marked chromosome pieces to analyze the effect of the disease on cells.

Sub
B3
A3

16. (Amended) A method suitable for facilitating diagnosis of Alzheimer's disease, the method comprising the steps of:

- exposing cells thought to be affected by Alzheimer's disease to a chromosome damaging agent;
- exposing the cells thought to be affected by Alzheimer's disease to a chromosome breakage agent to form chromosome pieces;
- marking at [lease] least some of the chromosome pieces within the cells' nuclei;
- and
- measuring an amount of marked chromosome pieces.

17. (Amended) The method suitable for facilitating diagnosis of Alzheimer's disease of claim 16, the method further comprising the steps of:

- exposing cells thought to be unaffected by Alzheimer's disease to a chromosome damaging agent;
- exposing the cells thought to be unaffected by Alzheimer's disease to a chromosome breakage agent to form chromosome pieces;
- marking at [lease] least some of the chromosome pieces of cells thought to be unaffected by Alzheimer's disease;
- measuring an amount of marked chromosome pieces present within the [cells] cells' nuclei thought to be unaffected by disease; [and]

Q3
cont
comparing a number of marked chromosome pieces present in the cells thought to be affected by the disease to a number of marked chromosomes pieces present in the cells thought to be unaffected by the disease[.]; and

determining diagnosis from said comparing step.

REMARKS

In the May 31, 2000 Office Action, the Examiner rejected all pending claims 1-17. After entry of the foregoing amendments, claims 1-17 remain pending in the application. Applicant respectfully requests reconsideration of all pending claims and earnestly solicits allowance of claims 1-17.

Claim Objections

The Examiner objected to claims 16 and 17. Claims 16 and 17 have been amended to obviate the objection. Applicant therefore requests that the Examiner withdraw the objection.

35 U.S.C. §112 Rejections

Claims 1-17 stand rejected under 35 U.S.C. § 112, first paragraph, for purportedly not being enabled. More specifically, the Examiner states that the specification does not provide enablement for diagnosing *any* disease by exposing cells of a suspected diseased patient to any chromosome damaging agent, marking some of the chromosome fragments, and analyzing the fragments to determine whether cells were affected by the disease nor for diagnosing Alzheimer's disease by exposing cells of a suspected diseased patient to a chromosome damaging agent, marking some of the chromosome fragments, and analyzing the fragments to determine whether cells were affected by the disease. Applicant traverses this rejection.

As a preliminary matter, Applicant submits that in general and as a matter of law, claims meet the requirement of enablement, even though they list elements that could form inoperative end products. *Atlas Powder Co, v, E.I. du Pont de Nemours & Co.*, 750 F.2d 1569 (Fed. Cir. 1984). Accordingly, Applicant submits that this non-enablement rejection is improper. Nevertheless, in an effort to further prosecution of the Application, Applicant has herein amended claims such that each of the pending independent claims 1, 11, and 16 is directed to a disease diagnosis method for analyzing cells "for which chromosome damage is diagnostic" (claim 1); "suspected of being affected by a disease for which chromosome damage is

diagnostic” (claim 11) and “thought to be affected by Alzheimer’s disease” (claim 16). Each independent claim 1, 11, and 16 recites a method for analyzing a disease for which chromosome damage is indicative of the presence of the disease, rather than *any* disease. Accordingly, Applicant requests that the Examiner reconsider and withdraw her rejection based on non-enablement of diagnosis of *any* disease.

The Examiner also states that gender differences exist in the study of genetic instability in Alzheimer’s disease, citing Cherry et al. Applicant submits that the results found in Cherry et al. have little relevance to the claimed invention and therefore traverses this rejection. The lack of observable difference between males and females in the Cherry et al. study may be attributable to, among other things, the use of chemicals other than those used by Applicant and described in the present application. Moreover, Cherry et al. did not employ caffeine to potentiate the effect of the treatment. Applicant submits that Parshad et al. teaches that, in the presence of caffeine, the differential induction of breakage in Alzheimer patients compared to controls can be observed in both males and females. Applicant further notes that it is permissible for a method claim to recite some condition or property without reciting in the claim every step necessary to obtain or achieve that condition or property. *In re Roberts and Burch*, 176 U.S.P.Q. (C.C.P.A. 1973).

The Examiner also states that the art teaches that not all strand-breaking agents induce chromosomal instability, citing Limoli et al. Applicant submits that the results found in Limoli et al. are not relevant to the claimed invention. In particular, Limoli et al. describes breakage induction in established cell cultures of rodent-human hybrid cells, which are expected to behave much differently from “patient cells” as set forth in claims 1, 11, and 16. Furthermore, the method used in Limoli et al. differs from the process described and claimed in the present application. For example, nowhere does Limoli et al. teach or suggest the use of caffeine to potentiate any damaging effect of the agents.

Claims 1-10 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, for purportedly failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. More particularly, the Examiner rejected claims 1-10 because the steps purportedly do not relate back to the preamble. Applicant disagrees. As the Examiner states, the preamble recites “a method suitable for facilitating disease diagnosis.” Applicant submits that any one of the steps listed in claim 1 may facilitate disease diagnosis, and

thus the elements properly relate back to the preamble. Moreover, the final step of claim 1, which includes “analyzing the marked chromosomes to determine whether the cells were affected by the disease” clearly relates to the preamble of claim 1. As noted above, Applicant need not list every step in a process claim. Accordingly, Applicant requests that the Examiner withdraw this rejection to claims 1-10.

Claims 11-15 stand rejected as being indefinite because the claims purportedly do not recite a positive process step that relates back to the preamble and as being indefinite over the recitation “a method of analyzing an effect of disease on cells.” Applicant disagrees but nevertheless has herein amended claim 11, from which claims 12-15 depend, and therefore requests that this rejection be withdrawn.

The Examiner also rejected claims 1-17 as being indefinite over the recitation of “marking at least some of the chromosomal fragments” because it is unclear whether the fragments are labeled, separated, or stained. The Examiner further states that marking is not an art recognized term. Applicant disagrees. The examiner uses the term “marked” on page 9 of the present Office Action in reference to what is described in Cherry et al. Applicant admits that the term “marked” may refer to various forms of labeling, staining, and the like, but submits that such use is proper—applicant is allowed to broadly claim his invention. Accordingly, Applicant requests that the Examiner withdraw this rejection claims 1-17.

Claims 16 and 17 stand rejected as being indefinite because the claims purportedly do not recite a positive process step that relates back to the preamble. Applicant has herein amended claims 16 and 17 to obviate this rejection. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw her rejection of claims 16 and 17.

35 U.S.C. § 103 Rejections

Claims 1-4, 6-7, 11, and 13-17 stand rejected under 35 U.S.C. § 103 (a) as being unpatentable over Cherry et al. Applicant traverses this rejection. Cherry et al. does not disclose “analyzing the marked chromosome fragments within cell nuclei” as set forth in claim 1, from which claims 2-4 and 6-7 depend; “marking at least a portion of the chromosome pieces within the cells’ nuclei” as set forth in claim 11, from which claims 13-15 depend; or “marking at least some of the chromosome pieces within the cells’ nuclei” as set forth in claim 16, from which claim 17 depends. Rather, Cherry et al. teaches conventional cytogenetic techniques to count

chromosome damage of chromosomes outside the cells' nuclei—such techniques are relatively labor intensive and expensive. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw her rejection to claims 1-4, 6-7, 11, and 13-17.

Claims 1-2, 4, 11, 13-14, and 16-17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chen et al. Again, Applicant traverses this rejection. Chen et al. does not disclose “analyzing the marked chromosome fragments within cell nuclei” as set forth in claim 1, from which claims 2 and 4 depend; “marking at least a portion of the chromosome pieces within the cells' nuclei” as set forth in claim 11, from which claims 13-14 depend; or “marking at least some of the chromosome pieces within the cells' nuclei” as set forth in claim 16, from which claim 17 depends. In contrast to Applicant's claimed invention, Chen et al., similar to Cherry et al., discloses use of conventional cytogenetic techniques that involve chromosome preparation. Such labor intensive and expensive techniques are neither required nor claimed in the present application. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw her rejection to claims 1-2, 4, 11, 13-14, and 16-17.


Claims 1-6 and 11-17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Parshad et al. Applicant traverses this rejection. Similar to Chen et al. and Cherry et al., Prashad et al. does not disclose “analyzing the marked chromosome fragments within cell nuclei” as set forth in claim 1, from which claims 2-4 depend; “marking at least a portion of the chromosome pieces within the cells' nuclei” as set forth in claim 11, from which claims 12-15 depend; or “marking at least some of the chromosome pieces within the cells' nuclei” as set forth in claim 16, from which claim 17 depends. Thus, Applicant respectfully requests that the Examiner reconsider and withdraw this rejection to claims 1-6 and 11-17.

Claims 1-2, 6-11, and 13-15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Gorczyca et al. Applicant traverses this rejection. Gorczyca generally discloses a TdT labeling technique as applied to the study of apoptosis. Apoptosis is a physiological state of all cells, irrespective of disease status. Nowhere, as the Examiner acknowledges in the present Office Action, does Gorczyca et al. teach or suggest disease diagnosis methods as set forth in claims 1-2, 6-11, and 13-15. Accordingly, Gorczyca et al. does not teach or suggest each and every element of claims 1-2, 6-11, and 13-15. Applicant therefore requests that the Examiner reconsider and withdraw her rejection to claims 1-2, 6-11, and 13-15.

Finally, claims 8-10 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Cherry et al. in view of Gorczyca et al. Again, Applicant traverses this rejection because neither Cherry et al., Gorczyca et al., nor a combination thereof teach or suggest each and every element of claim 1, from which claims 8-10 depend. In particular, neither reference teaches or suggests "a method suitable for facilitating disease diagnosis" and "analyzing the marked chromosome fragments *within cell nuclei* to determine whether the cells were affected by the disease" as set forth in claim 1, from which claims 8-10 depend. Furthermore, neither reference provides any motivation to combine the references. Accordingly, Applicant submits that the Examiner has not met the requirements to establish that claims 8-10 are rendered obvious by the combination of Cherry et al. and of Gorczyca et al. Applicant therefore respectfully requests that the Examiner reconsider and withdraw this rejection to claims 8-10.

In view of the foregoing arguments, Applicant submits that all pending claims are allowable over the cited references. Applicant therefore earnestly solicits allowance of pending claims 1-17. The undersigned would welcome a telephone call at the telephone number listed below if such would advance prosecution of this application.

Respectfully submitted,

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